

REMARKS

Claims 1-12 and 14-17 are pending in this application. Claims 7-9 and 19-22 has been withdrawn by the examiner. Claim 13 has been cancelled without prejudice or disclaimer. Claims 1-6, 10-12 and 14-17 are currently under examination. Without acquiescing in any rejection, claim 1 is amended to clarify that the diagnostic method may be performed on the sample and as discussed herein. Support for the amendment can be found throughout the specification. For example, support for an endocervical fluid sample or a vaginal fluid sample is found in original claim 1. The basis for stating that the diagnostic method is a diagnostic immunoassay method is found throughout the specification, see for example, at page 4, lines 3-7, and page 4, in the section entitled "Sample Preparation". The basis for stating that the sample is treated with an agent that reduces direct inhibition of antibody-antigen interaction by sample components, or that reduces viscosity of the sample, is found for example at page 4, in the section entitled "Sample Preparation". Therefore, no new matter is introduced. The Office Action is discussed below:

Withdrawal of Anticipation and Obviousness Rejections:

Applicants thank the examiner for withdrawal of the Anticipation and Obviousness rejections of the claims in view of the response filed on January 9, 2009.

New Grounds of Rejections:

Written Description Rejection:

On pages 3-5 of the Office Action, the examiner rejects claims 1-6, 10-12, 14-17 under 35 U.S.C. 112, first paragraph, allegedly as failing to comply with the written description requirement.

The examiner asserts that claims are drawn to a method for preparing a sample obtained from a human patient for performing a diagnostic method to detect whether the patient has been infected with an infectious agent, wherein the sample is

an endocervical fluid sample or a vaginal fluid sample, wherein the method comprises the steps of: a) treating sample to reduce an inhibitory effect of the sample on the diagnostic method; and b) performing the diagnostic method in the presence of DNase.

The examiner alleges that the scope of the claims as set forth above is drawn to a vast genus of inhibitory effects associated with a given (unnamed) diagnostic method. In particular, the examiner alleges that the claims encompass all diagnostic methods that can be used to detect any and all infectious agents. The examiner asserts that the specification does not disclose what diagnostic methods can be used to detect a given infectious agent, what inhibitory effects are possible within a given test system, and what steps must be performed to reduce a given inhibitory effect.

Without acquiescing to the examiner's rejection, applicants amend claim 1, for clarity, to recite that the claimed method is for preparing an endocervical fluid sample or a vaginal fluid sample obtained from a human patient for performing a diagnostic immunoassay method to detect whether the patient has been infected with an infectious agent, and that the endocervical fluid sample or the vaginal fluid sample is treated with an agent to reduce an inhibitory effect of the sample on the diagnostic method, wherein the agent reduces direct inhibition of antibody-antigen interaction by components of the sample, or wherein the agent reduces viscosity of the sample. Step (b) of claim 1 also has been amended, for clarity, to recite performing a diagnostic immunoassay method.

Thus, the amended claims do not encompass all diagnostic methods that can be used to detect any and all infectious agents, but rather diagnostic immunoassay methods. The methods are also specific for the preparation of an endocervical fluid sample or a vaginal fluid sample. It is therefore clear that the methods of the invention, by reducing an inhibitory effect of the sample on the diagnostic immunoassay method, can be used for preparing an endocervical fluid sample or a vaginal fluid sample for any diagnostic immunoassay method.

Applicants clarify that the amended claims do not encompass a vast and undisclosed genus of inhibitory effects. The amended claim 1 is directed to method

for treating the sample with an agent that reduces direct inhibition of antibody-antigen interaction by components of the sample, or the viscosity of the sample. The inhibitory effects of vaginal fluid on antibody-antigen interaction are described at page 3, fourth complete paragraph, and page 4, section entitled "Sample Preparation". It is explained that inhibition can be through physically blocking the antibody and antigen from coming together, sequestration of the target antigen, or modification of charges on the antibody molecule adversely affecting its affinity. Inhibition of proper mixing and liquid flow is stated to be related to the inherent viscosity of vaginal fluid, mainly contributed by mucin levels and amounts of DNA in the sample. A variety of different suitable agents for reducing the recited inhibitory effects of the sample on the diagnostic immunoassay method are disclosed at pages 5-6 of the specification, including DNase, oxidizing agents, non-ionic alkyl glucosides, polyvinyl alcohol, and polyvinyl pyrrolidine. Thus, the specification does not lack disclosure of what inhibitory effects are possible within the claimed test system or in disclosing what steps must be performed to reduce the inhibitory effect as specified in the amended claims.

In view of the above, applicants request withdrawal of the written description rejection.

Enablement Rejection:

On pages 5-8 of the Office Action, the examiner rejects claims 1-6, 10-12 and 14-17 under 35 U.S.C. 112, first paragraph, allegedly as being non-enabling. The examiner acknowledges that the specification is enabling for a method for preparing an endocervical or vaginal fluid sample obtained from a human patient for performing a dipstick-based diagnostic method to detect whether the patient has been infected with *Chlamydia trachomatis* utilizing DNase and an oxidizing agent. However, the examiner asserts that the specification does not provide enablement for a method for preparing an endocervical or vaginal fluid sample obtained from a human patient for performing a diagnostic method to detect whether the patient has been infected with any infectious agent, and the inhibitory effects on the sample, and the reduction of an inhibitory effect on a sample.

The examiner concludes that the claims are only enabled for the use of DNase and oxidizing agents in dipstick based diagnostic assays, but not the full breadth of the present claims. The examiner asserts that the specification only discloses the efficacy of using DNase and hydrogen peroxide in optimizing samples for use in a dipstick based test. The examiner further alleges that the specification is not only silent to the inhibitory effects inherent in each assay, but also to any method for preparing a sample to detect any infectious agent.

Applicants respectfully disagree with the examiner and submit that the examiner has not provided sufficient evidence and reasons to question applicants' presumptively correct disclosure. Applicants refer to the MPEP that states:

In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224, 169 USPQ at 370.

Applicants note that the test for enablement is not whether experimentation is necessary, but whether any experimentation would be undue in view of what type and amount of experimentation is usual in the field.

According to *In re Bowen*, 492 F.2d 859, 862-63, 181 USPQ 48, 51 (CCPA 1974), the minimal requirement is for the examiner to give

reasons for the uncertainty of the enablement. This standard is applicable even when there is no evidence in the record of operability without undue experimentation beyond the disclosed embodiments. See also *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (citing *In re Bundy*, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981)).

See MPEP §2164.04 at 2100-198 (Rev. 6, September 2007).

Applicants submit that the examiner has not satisfied this burden in the first instance because the examiner does not address what would be 'due' experimentation. See *In re Brana*, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (holding that an examiner must provide evidence to reject on enablement grounds, and absent such evidence applicants should not be required to substantiate their presumptively correct disclosure to avoid a rejection under the first paragraph of §112).

Without acquiescing to the rejection and in order to expedite the prosecution, applicants amend claim 1 to clarify that the claimed methods are directed to treatment of endocervical fluid samples or vaginal fluid samples obtained from a human patient. As discussed above, the specification explains that vaginal fluid is inhibitory to the interaction between antibodies and their target antigen (see for example, page 4, lines 15-16). The examples in the present application also show that treatment of the endocervical fluid or vaginal fluid sample in accordance with the claimed invention improves the quality of these samples to allow detection of infectious agents. *Chlamydia trachomatis* is simply one example of an infectious agent that can be detected following treatment of the sample. As will be apparent to the skilled person, there are many other diseases that can be detected by immunoassay, and since the quality of the sample for immunoassay is improved following treatment according to the invention, the methods described also will improve the detection of other infectious agents by immunoassay.

For the efficacies of using DNase and hydrogen peroxide, in addition to optimizing samples, applicants refer to the specification. For example, page 5 of the specification describes use of surfactants (non-ionic alkyl glucosides, particularly n-dodecyl maltoside) for increasing the availability of antigen for antibody detection, and use of PVP or PVA as an LPS carrier. Other agents for degrading nucleic acids and

other oxidizing agents are known to the skilled person and based on the teaching in the specification would be expected to improve the quality of the test sample for immunoassay.

Accordingly, withdrawal of the enablement rejection is solicited.

Anticipation/Obviousness Rejections:

On pages 8-9 of the Office Action, the examiner rejects claims 1 and 14 under 35 U.S.C. 102(b) allegedly as being anticipated by Bhattacharjee *et al.* (US Patent No. 5,919,617).

On pages 9-13 of the Office Action, the examiner rejects claims 1-6 and 14 under 35 U.S.C. 103(a) allegedly as being unpatentable over Bhattacharjee *et al.* (US Patent No. 5,919,617) in view of Bhattacharjee *et al.* (US Application No. 20030039981) and Switchenko *et al.* (US Patent No. 5,563,038).

On pages 13-17 of the Office Action, the examiner rejects claims 1, 10-12, and 14 under 35 U.S.C. 103(a) allegedly as being unpatentable over Bhattacharjee *et al.* (US Patent No. 5,919,617) in view of Sheiness *et al.* (US Patent No. 5,776,694), and Harada *et al.* (US Patent No. 4,251,643).

On pages 17-19 of the Office Action, the examiner rejects claims 1 and 14-17 under 35 U.S.C. 103(a) allegedly as being unpatentable over Sheiness *et al.* (US Patent No. 5,776,694) in view of Bhattacharjee *et al.* (US Patent No. 5,919,617).

Applicants respectfully disagree with the examiner and submit the following in order to assist the examiner in distinguishing the claimed invention from the cited references or any combinations thereof.

Regarding claims 1 and 14 and Bhattacharjee et al (US Patent No. 5,919,617):

Applicants clarify that the cited disclosure of Bhattacharjee relates to detection of fungal pathogens using hybridization methods. Since claim 1 has been amended to

recite performing a diagnostic immunoassay method, the cited disclosure of Bhattacharjee does not anticipate the subject matter of the amended claims. Whilst Bhattacharjee discloses methods of using antibodies to detect a fungal pathogen in a biological sample, there is no disclosure of performing such assays in the presence of DNase. Accordingly, the anticipation rejection should be withdrawn.

Regarding claims 1-6 and 14 and Bhattacharjee et al (US Patent No. 5,919,617) in view of Bhattacharjee et al (US Application No. 2003/0039981) and Switchenko et al (US Patent No. 5,563,038):

In particular, the examiner alleges that Switchenko et al teaches a method for detecting antigens in a clinical swab sample wherein the cell membrane components that are separated by solubilization with detergents (such as hydrogen peroxide) can be reconstituted. The examiner appears to consider that hydrogen peroxide is an example of a detergent described by Switchenko. However, it is clear from the disclosure of Switchenko that it is directed to a method for removal of detergents by chemically modifying the detergent to modify or destroy its detergent properties (column 6, lines 43-45). The detergent includes a modifiable group (column 5, lines 43-46) which is chemically modified by a modifying agent, such as hydrogen peroxide (column 6, lines 22-24). Thus, hydrogen peroxide is not a detergent, but a modifying reagent that creates free radicals and is used to destroy a detergent, and so Switchenko teaches use of oxidizing agents for removal of a detergent added to a sample. There is no disclosure that oxidizing agents may be used to treat the sample itself to reduce an inhibitory effect of the sample on a diagnostic immunoassay method. There is also no disclosure in Switchenko (or Bhattacharjee et al (US 5,919,617 and US 2003/0039981) of performing a diagnostic immunoassay method in the presence of DNase. Therefore, a process by combining the cited references would not disclose all claim limitations. Thus, no combination of the cited references can render the claimed subject matter unpatentable.

In this context, applicants request the examiner to consider the dictates of the MPEP that the applied references must teach or suggest all claim limitations.

Applicants submit that the rejections do not meet this test and refer the examiner that:

"All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

See, MPEP § 2143.03 at 2100-142 (Rev. 6, September 2007).

Regarding claims 1, 10-12 and 14 and Bhattacharjee et al (US Patent No. 5,919,617) in view of Sheiness et al (US Patent No. 5,776,694) and Harada et al (US Patent No. 4,251,643):

The examiner acknowledges that Bhattacharjee et al (US 5,919,617) does not teach a method wherein the sample is treated with either or both PVA and PVP, but alleges that Sheiness et al teach a method comprising treating a sample with PVP.

Sheiness et al relates to methods for releasing nucleic acid from a microorganism. The cited reference to PVP in this document (column 31, lines 24-29) relates to inclusion of PVP in a hybridization/slot blot solution. Use of this solution is described in Example 6 for hybridization of a labeled oligonucleotide with filters fixed with released RNA (column 40, lines 7-15). There is no disclosure of treatment of an endocervical fluid sample or a vaginal fluid sample with PVP. There is also no disclosure of diagnostic immunoassay methods in this document.

Regarding Harada et al, the examiner alleges that it would have been obvious to one of skill in the art to modify the method of Bhattacharjee et al by incorporating PVA for detecting the antigens in a biological sample (as disclosed by Switchenko et al) as an adhesive by embedding and preserving particles in a sample to detect organisms. The examiner's citation of this document is perplexing. It appears to have been cited simply because it contains the term "polyvinyl alcohol", without any consideration by the examiner as to the teaching of this document. The examiner does not point to any teaching in Harada that would have led the skilled person to use PVA as an adhesive to embed and preserve particles, and the examiner makes no

suggestion as to how this would reduce an inhibitory effect of the sample on the diagnostic method. There is no teaching in Harada that treatment of endocervical fluid samples or vaginal fluid samples with PVA could reduce the inhibitory effect of the sample on a diagnostic immunoassay. Indeed, use of the absorbent materials described by Harada in a method of the invention would be expected to severely inhibit an immunoassay, since they would absorb water from the sample, thereby inhibiting the immune reaction.

In this context applicants submit, if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)"

Accordingly, there is no suggestion or motivation for combining the cited references. Therefore, a *prima facie* case of obviousness has not been established by the examiner.

Moreover, since neither Sheiness et al nor Bhattacharjee et al (US 5,919,617) nor Harada et al disclose performing diagnostic immunoassay methods in the presence of DNase, and there is no disclosure in any of these documents of treatment of an endocervical fluid sample or a vaginal fluid sample with PVP or PVA, even if the cited references were combined, the resulting process would not disclose all claim limitations. Thus, no combination of the cited references can render the claimed subject matter unpatentable.

Finally, regarding claims 1 and 14-17 and Sheiness et al (US Patent No. 5,776,694) in view of Bhattacharjee et al (US Patent No. 5,919,617):


As explained above, neither Sheiness et al nor Bhattacharjee et al (US 5,919,617) disclose performing diagnostic immunoassay methods in the presence of DNase. Thus, no combination of the cited references can render the claimed invention obvious.

In view of the above clarifications and amendment to claim 1, applicants request withdrawal of the anticipation and obviousness rejections.

REQUEST

Applicants submit that claims 1-6, 10-12, and 14-17 are in condition for allowance and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



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